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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/540,296	01/20/2006	Maria Acelia Marrero Miragaya	976-28 PCT/US	3363

23869 7590 10/26/2007

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EXAMINER	
MACAULEY, SHERIDAN R	
ART UNIT	PAPER NUMBER
1651	
MAIL DATE	DELIVERY MODE
10/26/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/540,296	MARRERO MIRAGAYA ET AL.	
	Examiner	Art Unit	
	Sheridan R. MacAuley	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 May 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *21-25* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *21-25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *21 June 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *9/21/2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

A preliminary amendment was received and entered on July 21, 2005. Claims 1-20 were cancelled. Claims 21-25 are pending and examined on the merits in this office action.

Information Disclosure Statement

The information disclosure statement filed September 21, 2005 fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each cited foreign patent document; each non-patent literature publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. The information disclosure statement has been placed in the application file, but the foreign patent documents and non-patent literature publications referred to therein have not been considered.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> **The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.**

2. Claims 21-25 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

3. Claims 21-25 provide for the use of peptides and proteins with thrombolytic action but, since the claims do not set forth any steps involved in the method/process, it

is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

4. Claim 21 is rejected because it is unclear what applicant is intending to claim. Claim 1 recites the use of the claimed proteins to manufacture a medicament for treating a disease in a subject. It is unclear whether applicant intends to claim a method of manufacturing a medicament, a method of using a medicament, or a composition comprising the medicament.

5. In claim 21, the term "occlusive peripheral vascular disease, hemorrhoid disease" also renders the claim indefinite. It is unclear whether applicant intends to claim occlusive peripheral vascular disease and hemorrhoid disease, occlusive peripheral vascular disease or hemorrhoid disease, or some other option.

6. A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. See MPEP § 2173.05(c). Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131

USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949). In the present instance, claim 21 recites the broad recitation occlusive peripheral vascular disease, but the claim also recites hemorrhoid disease and occlusion of hemorrhoidal vessels and disorders associated with these diseases, which are the narrower statements of the range/limitation.

7. Claims 22-25 recite the limitations "claim 1" and "claim 4". There is insufficient antecedent basis for this limitation in the claims because each of the claims depend upon a cancelled claim. Thus, it is unclear which claim applicant intends for these claims to further limit. For examination purposes, and in the interest of compact prosecution, it has been assumed that applicant intended for claims 22-24 to depend from claim 21 and for claim 25 to depend from claim 24.

8. The term "UI/g" in claim 25 is a relative term that renders the claim indefinite. The term "UI/g" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. Enzyme activity units are measured differently depending upon different enzyme preparations and laboratory protocols. Since applicant has not described how the units of the instant claim are to be determined, the metes and bounds of the claim would be unclear to one of ordinary skill in the art.

Claim Rejections - 35 USC § 101

9. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

10. Claims 21-25 are rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Claim Rejections - 35 USC § 102

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

12. Claims 21-23 are rejected under 35 U.S.C. 102(b) as being anticipated by Gelfand (US 5,837,688). Claim 21 recites the use of peptides and proteins with thrombolytic action for the manufacture of a medicament for treating occlusive peripheral vascular disease, hemorrhoid disease, in particular the occlusion of hemorrhoidal vessels and disorders associated with these diseases in a subject, by rectal route. Claim 22 recites the use according to claim 1 wherein the medicament is a rectal formulation. Claim 23 recites the use according to claim 1 wherein the medicament comprises peptides and proteins where at least one of the components is a clot-lytic agent.

13. Gelfand teaches the manufacture of medicament compositions comprising peptides and proteins with thrombolytic action (e.g. streptokinase, which has activity that results in the degradation of fibrin clots) for the treatment of vascular disease, including disorders associated with occlusive peripheral vascular disease (abstract). Gelfand teaches that these compositions may be formulated in rectal compositions containing a carrier that is pharmacologically acceptable for rectal administration (col. 8, lines 50-53).

14. Therefore, Gelfand anticipates all of the limitations of the cited claims.

15. Claims 21-25 are rejected under 35 U.S.C. 102(b) as being anticipated by Baldwin et al. (US 5,098,707). Claim 21 recites the use of peptides and proteins with thrombolytic action for the manufacture of a medicament for treating occlusive peripheral vascular disease, hemorrhoid disease, in particular the occlusion of hemorrhoidal vessels and disorders associated with these diseases in a subject, by rectal route. Claim 22 recites the use according to claim 1 wherein the medicament is a rectal formulation. Claim 23 recites the use according to claim 1 wherein the medicament comprises peptides and proteins where at least one of the components is a clot-lytic agent. Claim 24 recites the use according the claim 1 wherein the medicament comprises recombinant streptokinase and pharmacologically acceptable diluent carrier or excipient for rectal route. Claim 25 recites the use according to claim 4 wherein the medicament comprises recombinant streptokinase in a concentration from 50,000-1,500,000 UI/g.

16. Baldwin teaches the manufacture of medicament compositions comprising peptides and proteins with thrombolytic action (e.g. streptokinase, which has activity that results in the degradation of fibrin clots) for the treatment of vascular disease, including disorders associated with occlusive peripheral vascular disease (abstract; col. 24, lines 1-35). Baldwin teaches that these compositions may be formulated in rectal compositions containing a carrier that is pharmacologically acceptable for rectal administration (col. 24, lines 32-35). Baldwin teaches that the streptokinase that is used in the composition may be of recombinant origin (col. 4, lines 8-17). Baldwin teaches that 1,500,000 units of streptokinase may be used in the composition (col. 24, lines 13-19).

17. Therefore, Baldwin teaches all of the limitations of the cited claims.

Claim Rejections - 35 USC § 103

18. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

19. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.

4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

20. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

21. Claims 21-25 rejected under 35 U.S.C. 103(a) as being unpatentable over Gelfand (US 5,837,688) in view of Baldwin et al. (US 5,098,707). Claim 21 recites the use of peptides and proteins with thrombolytic action for the manufacture of a medicament for treating occlusive peripheral vascular disease, hemorrhoid disease, in particular the occlusion of hemorrhoidal vessels and disorders associated with these diseases in a subject, by rectal route. Claim 22 recites the use according to claim 1 wherein the medicament is a rectal formulation. Claim 23 recites the use according to claim 1 wherein the medicament comprises peptides and proteins where at least one of the components is a clot-lytic agent. Claim 24 recites the use according the claim 1 wherein the medicament comprises recombinant streptokinase and pharmacologically acceptable diluent carrier or excipient for rectal route. Claim 25 recites the use according to claim 4 wherein the medicament comprises recombinant streptokinase in a concentration from 50,000-1,500,000 UI/g.

22. Gelfand teaches the manufacture of medicament compositions comprising peptides and proteins with thrombolytic action (e.g. streptokinase, which has activity that results in the degradation of fibrin clots) for the treatment of vascular disease, including disorders associated with occlusive peripheral vascular disease (abstract). Gelfand teaches that these compositions may be formulated in rectal compositions containing a carrier that is pharmacologically acceptable for rectal administration (col. 8, lines 50-53). Gelfand does not specifically teach the use of a recombinant streptokinase, or the use of the claimed amount of enzyme in the composition.

23. Baldwin teaches the manufacture of medicament compositions comprising peptides and proteins with thrombolytic action (e.g. streptokinase, which has activity that results in the degradation of fibrin clots) for the treatment of vascular disease, including disorders associated with occlusive peripheral vascular disease (abstract; col. 24, lines 1-35). Baldwin teaches that these compositions may be formulated in rectal compositions containing a carrier that is pharmacologically acceptable for rectal administration (col. 24, lines 32-35). Baldwin teaches that the streptokinase that is used in the composition may be of recombinant origin (col. 4, lines 8-17). Baldwin teaches that 1,500,000 units of streptokinase may be used in the composition (col. 24, lines 13-19).

24. At the time of the invention, the manufacture of a composition comprising nearly all of the claimed elements was known, as taught be Gelfand. It was also known that recombinant streptokinases could be used in compositions formulated for rectal administration in amounts similar to the claimed amounts, as taught by Baldwin. One of

ordinary skill in the art would have been motivated to use a recombinant streptokinase in the claimed amount in such a composition because Gelfand teaches that the effective dose of enzyme in the composition is determined based upon the formulation and route of administration (col. 4, lines 10-60). Since Baldwin teaches an amount of streptokinase that is acceptable for a similar formulation, one of ordinary skill in the art would have recognized that the amount taught by Baldwin could be used and varied over the course of routine experimentation to arrive at a composition with the claimed amount of streptokinase. One of ordinary skill in the art would have had a reasonable expectation of success in combining these teachings because both teach the manufacture of a composition comprising streptokinase that is suitable for use with multiple carriers for rectal administration. It would therefore have been obvious to one of ordinary skill in the art to combine the teachings discussed above to arrive at the claimed invention.

25. Thus, the claimed invention as a whole was *prima facie* obvious over the combined teachings of the prior art.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sheridan R. MacAuley whose telephone number is (571) 270-3056. The examiner can normally be reached on Mon-Thurs, 7:30AM-5:00PM EST, alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on (571) 272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

SRM
/Ruth A Davis/
Primary Examiner, AU 1651